REMARKS/ARGUMENTS

In the August 9, 2005 Office Action, the Examiner rejected claims 31-33, 35-40, 42, 44-46 and 48 pending in the application. This response cancels claims 32, 35-36, 38, 40, 42, 45 and 48, without prejudice or disclaimer, and amends claims 31, 33, 37 and 39 for consideration. After entry of the foregoing amendments, claims 31, 33, 37, 39, 44 and 46 (2 independent claims; 6 total claims) remain pending in the application. Reconsideration is respectfully requested.

Claims 31-33, 35 and 36 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Papac et al. (Analytical Chemistry) in view of Gaskell (Quantification of Steroid Conjugates Using Fast Atom Bombardment Mass Spectrometry, Steroids, 1990, Vol. 55, pages 458-462). In particular, the Examiner states that Papac discloses a method for the mass spectral identification and detection of analytes separated by immunoaffinity chromatography, using antibody immobilized agarose beads as affinity columns, combining a specimen with the beads to capture antigen present in the sample (post-combination affinity reagent), washing to remove any unbound antigen, mixing sample with the beads and centrifuging and removing supernatant, adding a matrix containing formic acid to the supernatant and testing by MALDI-TOF mass spectrometry (single dimension mass spectrometric analysis), and determining the analyte by mass-to-charge ratio. Although the Examiner concedes that Papac fails to teach that the specimen is combined with an internal reference species of known concentration prior to capturing and isolating the analyte and IRS, and also failing to teach quantifying the analyte, the Examiner contends that Gaskell discloses quantifying an analyte where a deuterated internal standard is added to the sample which is then mixed with the solid phase incorporating bound antiserum for isolating the analyte and internal standard. The Examiner further contends that Gaskell discloses that for quantification of the analyte, the analyte and the internal standard are compared to a standard curve and that the standard curve was obtained by analysis of standard mixtures of the analyte and analyte analog. The Examiner also asserts that Gaskell discloses that the addition of an internal standard provides for precise and accurate data and provides for the quantification of an analyte. Accordingly, the Examiner contends that it would have been obvious to one of ordinary skill in the art to incorporate an internal standard and affinity reagent and also to develop a standard curve for quantification analysis into the method of Papac because Gaskell teaches that the addition of an internal standard provides for precise and accurate data and provides for the quantification of an analyte of interest. The Examiner further contends that

one of ordinary skill in the art would have had a reasonable expectation of success by incorporating an internal standard and affinity reagent as taught by Gaskell into the method of Papac. Applicants respectfully traverse this rejection with respect to remaining claims 31 and 33.

First, the capturing and isolating of at least one or more analyte is performed completely differently than the process described in Papac. In particular, Papac fails to disclose releasing an isolated analyte species by eluting the analyte species from an antibody and then detecting the presence of the isolated and released analyte species using a mass spectrometer. Instead, aliquots of beads containing the predetermined analyte were removed from the column for performing MALDI/TOF analysis (see page 2611, column 1, first paragraph). The discussion under mass spectrometry on page 2611, first paragraph of the Papac reference merely describes how the sample aliquots of beads containing the known analytes were prepared for performing mass spectrometry. Further, this is clearly confirmed in the results and discussion section which states: "Purification was necessary before binding the antibody to the affinity support. To accomplish this purification, cytochrome c was first bound to the affinity support (see experimental section). The crude antibody solution was passed through the column, and a one-micro liter aliquot of the column bed was used to acquire the MALDI/TOF spectrum shown in Fig. 1A." (Papac, page 2611, bottom of column 1, top of column 2). In contrast, in Applicants' invention, the analyte species is released by eluting it from the antibody and a released analyte species is detected using a mass spectrometer to determine whether the analyte species is present in the physiological specimen, determining the identity of the analyte species using molecular weight analysis, and determining the quantity of the analyte species.

Moreover, the Gaskell reference cited by the Examiner discloses fast atom bombardment/mass spectrometry or liquid secondary ion mass spectrometry to analyze steroid conjugates (sulfates, gulcuronides) without prior hydrolysis or derivitization. In particular, the Gaskell reference describes the quantitative determination of dehydroepiandrosterone sulfate in serum by selective isolation of the analyte using immunoadsorption extraction and highly specific detection using tandem mass spectrometry. The quantification method includes 1) stable isotope dilution using an internal standard, 2) isolation of the analyte by immunoadorption, and 3) detection of both the analyte and internal standard during limited mass range parent ion scanning during tandem mass spectrometry (see page 460, column 1, fourth paragraph of the Gaskell reference). Furthermore, the Gaskell reference specifically states that "the success of the

detection procedure was dependent both on the selectivity of tandem MS detection and on the achievement of a sufficiently "clean" biologic extract by immunoadsorption." (See page 461, column 2, second paragraph of Gaskell). Accordingly, the Gaskell reference cited by the Examiner actually teaches away from the instantly claimed invention by using tandem MS for quantification. In other words, different mass spectrometric measurements were taken of similar portions of the same serum extract and compared. In contrast, in Applicants' instantly claimed invention, the analyte and IRS are measured using MS in a single measurement. Accordingly, it would not have been obvious to one of ordinary skill in the art to incorporate the method disclosed in Gaskell into the method of Papac to arrive at Applicants' claimed invention because Applicants' claimed invention would then require tandem MS. In contrast, Applicants' claimed invention requires single dimension MS.

Claims 37-40 and 42 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Papac et al. in view of Gaskell as applied to claims 31-33, 35 and 36 above, and further in view of Chiabrando et al. Applicants respectfully traverse this rejection with respect to remaining claim 37. As previously stated above, in contrast to Papac, the analyte species in Applicants' invention is released by eluting it from the antibody and a released analyte species is detected using a mass spectrometer to determine whether the analyte species is present in the physiological specimen. Applicants' invention then determines the identity of the analyte species using molecular weight analysis and the quantity of the analyte species. In addition, , it would not have been obvious to one of ordinary skill in the art to incorporate the method disclosed in Gaskell into the method of Papac to arrive at Applicants' claimed invention because Applicants' claimed invention would then require tandem MS. Further, Chiabrando also fails to disclose eluting the analyte species from an antibody and performing single dimension mass spectrometry. Therefore, it could not have been obvious to one of ordinary skill in the art to combine Papac, Gaskell, and Chiabrando, either alone or in combination, to arrive at Applicants' claim 37.

Claims 44-46 and 48 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Papac et al. and Gaskell in view of Chiabrando as applied to claims 31-33, 35-40, and 42 above, and further in view of Merren. Applicants respectfully traverse this rejection with respect to remaining claims 44 and 46. As previously stated above, in contrast to Papac, the analyte species in Applicants' invention is released by eluting it from the antibody and a released analyte species is detected using a mass spectrometer to determine whether the analyte species is present

in the physiological specimen. Applicants' invention then determines the identity of the analyte species using molecular weight analysis and the quantity of the analyte species. In addition, , it would not have been obvious to one of ordinary skill in the art to incorporate the method disclosed in Gaskell into the method of Papac to arrive at Applicants' claimed invention because Applicants' claimed invention would then require tandem MS. Further, both Chiabrando and Merren also fail to disclose eluting the analyte species from an antibody and performing single dimension mass spectrometry. Therefore, it could not have been obvious to one of ordinary skill in the art to combine Papac, Gaskell, Chiabrando, and Merren, either alone or in combination, to arrive at Applicants' claims 44 and 46.

In view of the foregoing, Applicants respectfully submit that all of the pending claims are allowable over the prior art of record. Reconsideration of the application and allowance of all pending claims is earnestly solicited. Should the Examiner wish to discuss any of the above in greater detail or deem that further amendments should be made to improve the form of the claims, then the Examiner is invited to telephone the undersigned at the Examiner's convenience. The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account No. **19-2814**. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

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in the physiological specimen. Applicants' invention then determines the identity of the analyte species using molecular weight analysis and the quantity of the analyte species. In addition, , it would not have been obvious to one of ordinary skill in the art to incorporate the method disclosed in Gaskell into the method of Papac to arrive at Applicants' claimed invention because Applicants' claimed invention would then require tandem MS. Further, both Chiabrando and Merren also fail to disclose eluting the analyte species from an antibody and performing single dimension mass spectrometry. Therefore, it could not have been obvious to one of ordinary skill in the art to combine Papac, Gaskell, Chiabrando, and Merren, either alone or in combination, to arrive at Applicants' claims 44 and 46.

In view of the foregoing, Applicants respectfully submit that all of the pending claims are allowable over the prior art of record. Reconsideration of the application and allowance of all pending claims is earnestly solicited. Should the Examiner wish to discuss any of the above in greater detail or deem that further amendments should be made to improve the form of the claims, then the Examiner is invited to telephone the undersigned at the Examiner's convenience. The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account No. **19-2814**. A duplicate copy of this sheet is enclosed.

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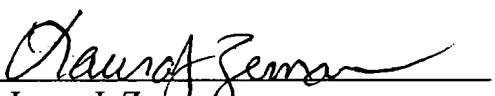
By: 
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